Deloitte & Touche

A STUDY OF STRATEGIC OPPORTUNITIES FOR CANADIAN BIOTECHNOLOGY IN ANIMAL HUSBANDRY PRODUCTS

Phase I Report

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A STUDY OF STRATEGIC OPPORTUNITIES FOR CANADIAN BIOTECHNOLOGY IN ANIMAL HUSBANDRY PRODUCTS

Phase I Report

For

INDUSTRY SCIENCE AND TECHNOLOGY CANADA

By

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TABLE OF CONTENTS

SECTION			PAGE
EXECUTIVE SUMMARY			i
1.0	INTRODUCTION		1
2.0	BACKGROUND		3
	2.1	A Conceptual Model of Biotech Applications	3
	2.2	Biotech Approaches	5
3.0	CURRENT AND PROSPECTIVE ANIMAL HUSBANDRY ISSUES		7
4.0	CURRENT BIOTECHNICAL RESEARCH WITH POTENTIAL APPLICATIONS FOR ANIMAL HUSBANDRY		14
	4.1	Immunization Modulation	14
	4.2	Chemical Modulation	19
	4.3	Transgenics	20
5.0	INITIAL ASSESSMENT OF MARKET OPPORTUNITIES		22
6.0	SUMMARY		32
7.0	A FRAMEWORK FOR PHASE II		34

LIST OF TABLES

Table 3.1	Animal Husbandry Issues - Dairy	10
Table 3.2	Animal Husbandry Issues - Beef	11
Table 3.3	Animal Husbandry Issues - Swine	12
Table 3.4	Animal Husbandry Issues - Equine	13
Table 5.1	Potential Domestic Benefits	24
Table 5.2	Biotech Product Research Stages	29

LIST OF FIGURES

Figure 2.1	Interaction of Product Development Process and Biotechnology	4
Figure 2.2	Animal Husbandry - Strategies, Effects and Applications	6
Figure 4.1	Major Process in Immunization Modulation	17

EXECUTIVE SUMMARY

1. The potential benefits of biotechnology in the animal husbandry sector are in the billions of dollars. When the spin-off effects of research are considered, i.e. the potential application of similar techniques to other species including humans, the potential benefits increase dramatically.

2. The potential applications for products of biotechnology in the animal husbandry sector are virtually unlimited. Disease control and resistance, and enhancing production characteristics and abilities are the major applications.

3. These huge potential commercial benefits must be qualified by the high cost of research and product development. The costs of doing business in the biotech area is much higher than conventional research. Availability of capital is one of the major limiting factors to biotech research firms and institutions.

4. Canada is at the leading edge of technology in several areas of biotechnology, most notably in the areas of embryology and immunization technology.

5. Few biotechnology products are ready for market as yet. Much of the research is still focusing on understanding the processes, mapping the genes, and laying the ground work for specific applications.

6. For the industry to develop as a whole, and for Canada to play a strong role, a strong multi-disciplinary approach ,and a high degree of industry coordination will be required.

1.0 INTRODUCTION

The Department of Industry, Science and Technology (ISTC) seeks to identify strategic opportunities for Canada in the application of biotechnology to the animal husbandry sector.

The National Biotechnology Advisory Committee (NBAC) advises the Minister of Industry, Science and Technology on ways and means of using biotechnology to develop and maintain the competitiveness of Canadian industry. Recently the NBAC has established three Working Groups to address different aspects of biotechnology growth in Canada. One of these, the Working Group for Agribusiness and Food has determined, through a preliminary survey of companies prominent in the Canadian agriculture and food sectors, that opportunities for growth might be found in the development of improved veterinary products. It is anticipated that these opportunities will lie mainly in two areas. One of them is in the development of genetically engineered vaccines for the treatment of endemic diseases of large animals. The other is in novel hormonal treatments for improved feed efficiency and utilization, and faster more productive animal growth.

Consequently, Deloitte & Touche has been commissioned by ISTC to identify the most significant niche opportunities for biotechnology based development within the animal husbandry area.

This report presents the findings of the first phase of the project. The objective of this phase was:

1. to identify and list the major issues/products/techniques of significance to the biotech industry; and

2. to provide an initial assessment of the commercial significance of these areas and desirability of further research.

The approach used in this phase of the study consists of three steps. The first was to identify major issues in the area of dairy, beef, swine and equine animal husbandry in order to define the universe of applications available for biotech products. The second step was to overview the research taking place in Canada today and potential applications in order

to define the capabilities of the Canadian biotech sector. The third step was to provide an initial assessment of the opportunities, that is, the relationship between the issue or market need, and our ability to address this need vis-a-vis other competitive factors was assessed within an industry competitiveness framework.

The report is based on interviews with scientists and business people, reviews of published research papers, articles and statistics and a review of in-house market information.

The report is organized as follows: Chapter 2 discusses some of the background issues to the study, and the conceptual model on which the study is based. Chapter 3 discusses the major issues in animal husbandry for each of the sectors of interest in this study. Chapter 4 outlines the current and prospective research taking place in Canada, as well as the potential market applications for this research. Chapter 5 discusses relative market opportunities. Chapter 6 summarizes the findings of the research and Chapter 7 presents a framework for further research.

2.0 BACKGROUND

The initial terms of reference for this project stated that the contractors were to identify the specific opportunity areas for development of:

a) high efficiency, genetically engineered, large animal vaccines to combat endemic diseases in large animals (dairy, beef, swine and horses) that are not well served by available treatments; and

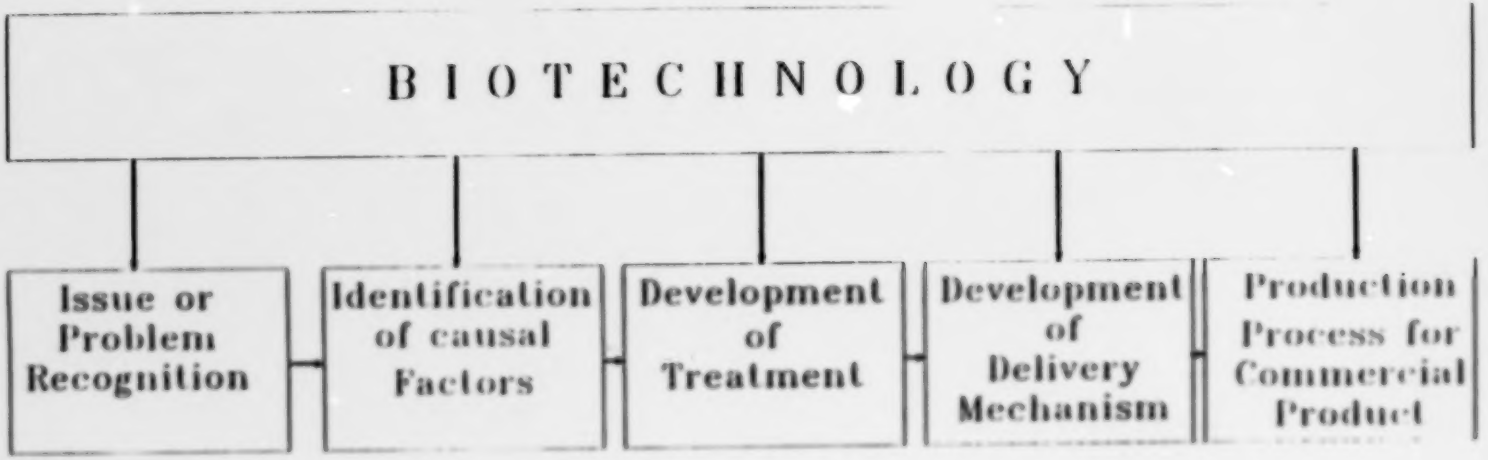
b) hormonal treatments for growth promotion and feed efficiency improvement in large animal species.

The initial round of discussions with industry and researchers showed that there may be other significant biotechnology market opportunities within the area of animal husbandry which are not covered by this definition. Consequently, it was decided that any biotechnical application which had a direct impact on the husbandry of large animals would be considered.

2.1 A Conceptual Model of Biotech Applications

Before we can assess the market opportunities for specific products, it is necessary to understand the process by which the tool of biotechnology interacts with the process of developing and producing a product with commercial potential. Biotechnology can be defined as "the goods and services provided by cells and cell products" and can have applications at several stages of the product development process. As such, biotechnology is not a product or a discipline, but is more of a tool or approach whereby the cell is used as a mechanism, (which may be used alone or in combination with other cells) to achieve specific ends. Figure 2.1 shows the stages during the product development process where biotechnology can play a role.

FIGURE 2.1
INTERACTION OF PRODUCT DEVELOPMENT PROCESS AND BIOTECHNOLOGY



2.2 Biotech Approaches

Three basic mechanisms through which biotechnology can be applied to the area of animal husbandry have been identified. These are:

1. Immunization Modulation

   The process of modifying the immune system of the target species to achieve the desired results. Most commonly used in development of vaccines for disease control but immunization agents may also be used to alter metabolic pathways and affect performance characteristics.

2. Chemical Modulation

   The process of modifying microbes to produce chemicals which then interact with the target species to achieve the desired results. The use of E. coli to produce Bovine Somatotropin is an example of this process.

3. Transgenics

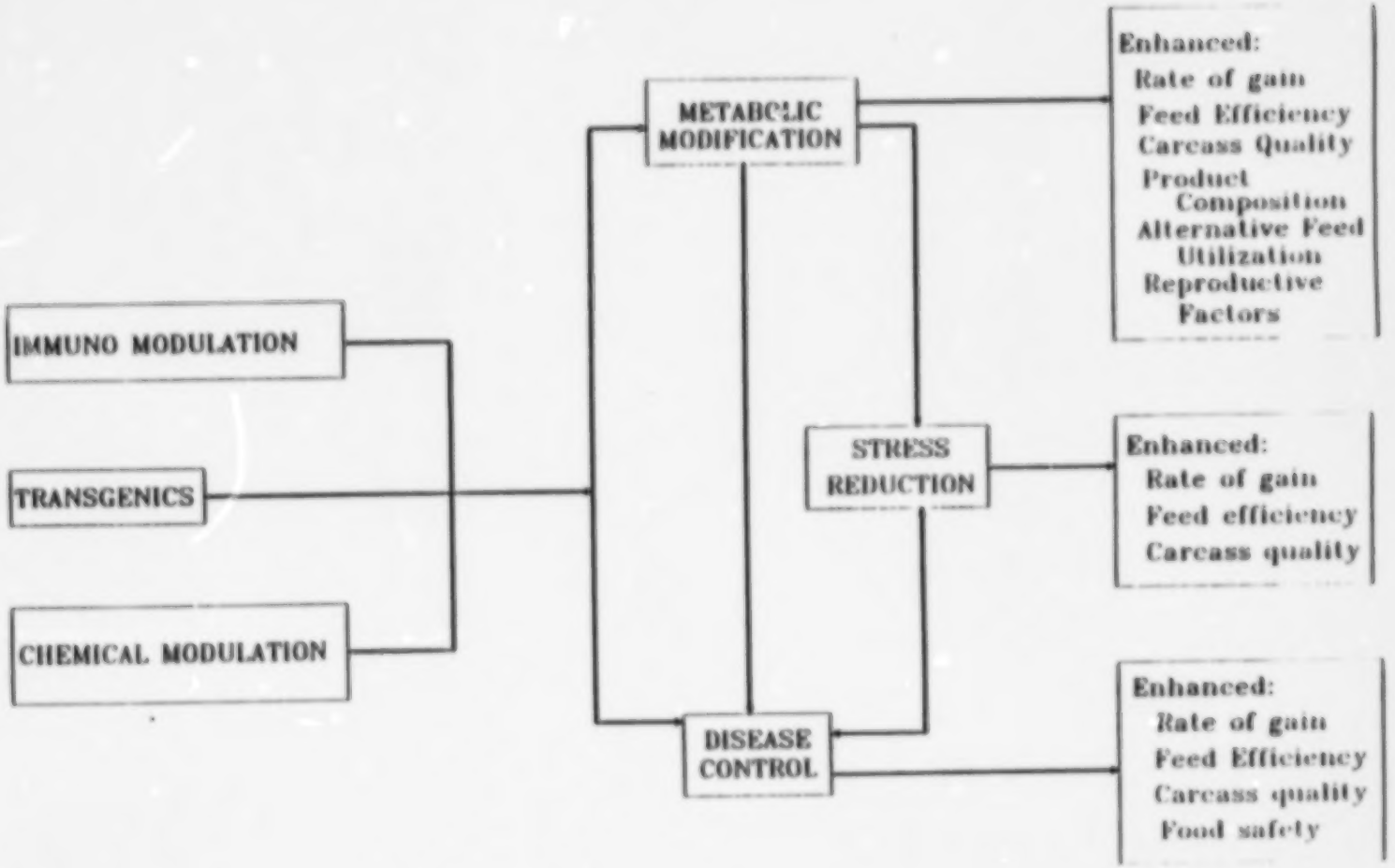
   Transgenics is the manipulation of the genetic material to implant or remove the specific gene or genes responsible for producing targeted characteristics.

Within each of these mechanisms there can be a wide variety of approaches to specific animal husbandry issues. Additionally, the three mechanisms may offer potential solutions to the same individual issues, albeit through radically different pathways.

The pathways by which these three processes can have an impact on specific animal husbandry issues (e.g. enhanced rate of gain) is shown diagrammatically in Figure 2.2.

FIGURE 2.2

ANIMAL HUSBANDRY - STRATEGIES, EFFECTS AND APPLICATIONS



3.0 CURRENT AND PROSPECTIVE ANIMAL HUSBANDRY ISSUES

This Chapter presents a review of the current animal husbandry issues for each of the species in question. For each species these issues, the animal husbandry objective, the current solutions (if any), and potential biotech solution are shown in Table 3.1 (dairy), Table 3.2 (beef), Table 3.3 (swine), and Table 3.4 (horses).

The major issues fall into similar categories for the dairy, beef and swine sectors, but are somewhat different in the equine area. This is to be expected as the common purpose of dairy, beef and swine production is food, while the reason for horse production is generally sport and recreation. It must be emphasized that each of these issues are the result of a number of factors. Hence, the opportunities for approaching each issue are multiple as well. Tables 3.1 - 3.4 also provide an idea of the potential biotechnical process (although not the potential pathways, which would be far too numerous to list) by which the issues may be addressed. The issues can be briefly described as follows:

Productivity/Rate of Gain

Productivity is the measure of the total product output per production unit, and usually implies a time dimension. Enhancing productivity is an issue because increasing productivity also increases gross returns. In addition, maximizing product output per unit of time contributes to efficient use of capital, that is, the fixed costs of production are spread over more units of production.

Feed Efficiency

Feed efficiency can be described as the relative ability of the animal to transform raw materials into a marketable product. The objective being to increase the units of marketable output per dollar of feed input. Maximizing output per kilogram of feed input may also be an issue. For example, the productivity of top producing dairy cows may be limited by their ability to consume the sheer quantity of feed necessary to support their potential production levels.

Utilization of Alternative Feeds

The potential ability of food producing animals to utilize alternative or non-traditional feeds has important applications from a number of aspects. First, it offers the prospect of lower cost of production if the alternative feeds can be produced or obtained more cheaply than those feeds currently used. Examples of this would include the feeding of legume hays to non-ruminants to lower the cost of the protein fed. A second potential application is in the area of expanding livestock production into areas which, for agronomic reasons, cannot grow the traditional feeds.

Product Composition

The issue of the composition of the product, be it meat or milk has three elements. The first relates to the consumer acceptance of the product, altering the fat composition (lipid profile) of meat to lower cholesterol could generate more demand for the product in total, and raise the value of the product vis-a-vis competing products. The second relates to the relative value of the constituent components, increasing the protein content of milk could be of direct benefit to the milk processing industry. The third relates to the potential for using the animal as an entity to produce novel products. For example, it may be possible to induce the mammary glands of cattle to produce specialized enzymes for use in other processes, and collect these enzymes from the milk.

Carcass Quality

The issue of carcass quality relates to the relative value and yield of the carcass components. Certain portions of the carcass, such as the tenderloin, rump or ham, have higher value, generally related to the amount of lean. By increasing the relative yield of these higher value cuts, total revenue per animal could also be increased.

Disease Control/Food Safety

Disease control is the most broadly scoped issue facing farmers today. The costs of poor disease control are manifested both at the farm level through increased costs of production and loss of revenue, and at the consumer level through the health aspects of eating contaminated foods. While this last issue may not be significant in Canada, it is much more important on a global scale. Another food safety issue is that of additives currently used in the production of livestock. Consumer perceptions of antibiotic and growth promotant usage may have a detrimental impact on the market for livestock products. By using biotechnical processes, the need for some of these other products may be circumvented, and consumer concerns alleviated.

TABLE 3.1 ANIMAL HUSBANDRY ISSUES - DAIRY

ISSUE	OBJECTIVE	PRESENT SOLUTION	BIOTECH OPPORTUNITY/PROCESS
Productivity	Increase Kg's milk/day/cow	1. Enhanced nutritional management 2. Conventional breeding strategies 3. Embryo transfer	1. Control of metabolic pathway through immunilogical or chemical mechanisms such as BST 2 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3 transgenic manipulation to obtain or enhance desired traits
Feed Efficiency	Increase milk production per $/feed	1. Ration balancing 2. Conventional breeding strategies and embryo transfer 3. Use of higher quality feeds 4. Improved animal health status	1. Control of metabolic pathway through immunilogical or chemical mechanisms such as BST 2 Microbial enhancement of feeds 3. Transgenic manipulation to obtain or enhance desired traits 4 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning
Utilization of Alternative Feeds	Lower production costs through use of non-traditional feedstuffs	1. Ensiling agents	1. Genetically engineered microbes & chemicals applied internally or to the feed, to enhance palatability, nutrition or digestability of alternative feeds
Product Composition	Increase proportions of desirable components in the product, such as protein	1. Conventional breeding strategies and embryo transfer	1. Transgenic manipulation to obtain or enhance desired traits 2. Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3. Bio-engineering of feedstuffs or feed additives to enhance meat characteristics
	Utilize the animal for molecular manufacture with products expressed in the mammary gland and collected in the milk	1. None	1. Transgenics
Disease Control	Enhanced productivity and reduced mortality Develop Diagnostic Tools	1. Vaccines 2. Antibiotics 3. Environment management 4. Breeding for resistance	1. Engineered vaccines/antigens which cannot currently be produced economically or in pure enough form 2 Gene modification of microbes to produce chemicals to control disease 3 Transgenic alteration to enhance the animals ability to react to or resist the disease organism, or causative factor 4 development of gene markers to aid in conventional breeding for resistance

TABLE 3.2 ANIMAL HUSBANDRY ISSUES – BEEF

ISSUE	OBJECTIVE	PRESENT SOLUTION	BIOTECH OPPORTUNITY/PROCESS
Productivity	Raise Weaning Weights Shorten Days on Feed	1. Growth promotants such as hormonal implants, and ionophores 2. Enhanced nutritional management 3. Conventional breeding strategies 4. Embryo transfer	1. Control of metabolic pathway through immunological or chemical mechanisms 2 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3 transgenic manipulation to obtain or enhance desired traits
Feed Efficiency	Lower Kg's feed/Kg gain Lower cost of feed/kg of gain	1. Growth promotants such as hormonal implants, and ionophores 2. Enhanced nutritional management 3. Conventional breeding strategies 4. Embryo transfer	1. Control of metabolic pathway through immunological or chemical mechanisms 2 Microbial enhancement of feeds 3 Transgenic manipulation to obtain or enhance desired traits 4 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning
Carcass Quality	Increase yield of lean meat Increase the relative yield of high value cuts Improve meat texture	1. Conventional breeding strategies and embryo transfer 2. Nutrition management	1. Control of metabolic pathway through immunological or chemical mechanisms 2 Microbial enhancement of feeds 3 Transgenic manipulation to obtain or enhance desired traits 4 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning
Utilization of Alternative Feeds	Lower production costs through use of non-traditional feedstuffs	1. Ensiling agents	1 Genetically engineered microbes & chemicals applied internally or to the feed, to enhance palatability, nutrition or digestability of alternative feeds 2 Transgenic manipulation of the animal to alter the digestive process
Product Composition	Improve the composition of both the lean and fat components	1. Conventional breeding strategies and embryo transfer	1. Transgenic manipulation to obtain or enhance desired traits 2 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3 Bio-engineering of feedstuffs or feed additives to enhance meat characteristics
Disease Control	Enhanced productivity and reduced mortality Develop Diagnostic Tools	1. Vaccines 2. Antibiotics 3. Environment management 4. Breeding for resistance	1 Engineered vaccines/antigens which cannot currently be produced economically or in pure enough form 2 Gene modification of microbes to produce chemicals to control disease 3 Transgenic alteration to enhance the animals ability to react to or resist the disease organism, or causative factor 4 development of gene markers to aid in conventional breeding for resistance

TABLE 3.3 ANIMAL HUSBANDRY ISSUES – SWINE

ISSUE	OBJECTIVE	PRESENT SOLUTION	BIOTECH OPPORTUNITY/PROCESS
Productivity	Raise Weaning Weights Shorten Days to market Enhance sow productivity (increase # of piglets weaned per sow)	1. Growth promotants in feed, such as sub-therapuetic levels of antibiotics 2 Enhanced nutritional management 3. Conventional breeding strategies	1. Control of metabolic pathway through immunological or chemical mechanisms 2 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3 transgenic manipulation to obtain or enhance desired traits
Feed Efficiency	Lower Kg's feed/Kg gain Lower cost of feed/kg of gain	1. Growth promotants in feed, such as sub-therapuetic levels of antibiotics 2. Enhanced nutritional management 3. Conventional breeding strategies	1 Control of metabolic pathway through immunological or chemical mechanisms 2 Microbial enhancement of feeds 3 Transgenic manipulation to obtain or enhance desired traits 4 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning
Carcass Quality	Increase yield of lean meat Increase the relative yield of high value cuts Improve meat texture	1. Conventional breeding strategies and embryo transfer 2. Nutrition management	1 Control of metabolic pathway through immunological or chemical mechanisms 2 Microbial enhancement of feeds 3 Transgenic manipulation to obtain or enhance desired traits 4 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning
Utilization of Alternative Feeds	Lower production costs through use of non-traditional feedstuffs	1. Ensiling agents	1. Genetically engineered microbes & chemicals applied internally or to the feed, to enhance palatability, nutrition or digestability of alternative feeds 2 Transgenic manipulation of the animal to alter the digestive process
Product Composition	Improve the composition of both the lean and fat components	1. Conventional breeding strategies	1 Transgenic manipulation to obtain or enhance desired traits 2 Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 3 Bio-engineering of feedstuffs or feed additives to enhance meat characteristics
Disease Control	Enhanced productivity and reduced mortality Develop Diagnostic Tools	1. Vaccines 2. Antibiotics 3. Environment management 4 Breeding for resistance	1 Engineered vaccines/antigens which cannot currently be produced economically or in pure enough form 2 Gene modification of microbes to produce chemicals to control disease 3 Transgenic alteration to enhance the animals ability to react to or resist the disease organism, or causative factor 4 development of gene markers to aid in conventional breeding for resistance

TABLE 3.4 ANIMAL HUSBANDRY ISSUES - EQUINE

ISSUE	OBJECTIVE	PRESENT SOLUTION	BIOTECH OPPORTUNITY/PROCESS
Disease Control/ Animal Health	Enhance performance and reduce mortality Develop Diagnostic Tools	1. Vaccines 2. Antibiotics 3. Environment Management 4. Isolation and Avoidance	1. Engineered vaccines/antigens which cannot currently be produced economically or in pure enough form 2. Gene modification of microbes to produce chemicals to control disease 3. Transgenic alteration to enhance the animals ability to react to or resist the disease organism, or causative factor 4. development of gene markers to aid in conventional breeding for resistance
Reproductive Management	Improve Breeding efficiency/foaling rates	1. Hormonal inducement of ovulation 2. Nutritional Management 3. Health Management 4. Environment Management	1. Enhanced reproductive capability of superior animals through embryo sexing, splitting, preservation and cloning 2. Control of the metabolic process through immunological or chemical mechanisms
Performance	Improved strength, speed	1. Conventional breeding	1. Control of the metabolic process through immunological or chemical mechanisms to increase efficiency of energy conversion 2. Transgenic manipulation to obtain or enhance desired traits
Utilization of Alternative Feeds	Lower production costs through use of non-traditional feedstuffs		1. Genetically engineered microbes & chemicals applied internally or to the feed, to enhance palatability, nutrition or digestability of alternative feeds 2. Transgenic manipulation of the animal to alter the digestive process

4.0 CURRENT BIOTECHNICAL RESEARCH WITH POTENTIAL APPLICATIONS FOR ANIMAL HUSBANDRY

This chapter presents an overview of the types of research that are currently in progress in Canada in the area of biotechnical approaches to animal husbandry issues. The approach used in this chapter is to focus on the biotech process. It should be understood that biotechnology is a multidisciplinary science, and that each process is made up of a number of disciplines which could include veterinary microbiology, immunology, cell biology, and molecular biology, as well as numerous others. Similarly, the potential applications for products derived from each process are varied in nature. For example, the layman tends to think of immunization as a mechanism for disease control only. However, animals (and man) can be immunized against many metabolic factors that involve hormones, enzymes and toxins, and can thus can be key factors in managing many productivity factors as well.

Chapter 2 of this report introduced the three major processes involved in animal husbandry biotechnology - transgenics, immunization and chemical modulation. This chapter builds on these definitions to highlight the specific area of research and outline the variety of potential and specific products which may result from application of these processes.

For a variety of reasons, it is difficult to focus on specific products at this stage. First, the nature of biotechnical research is such that many commercial applications will be discovered serendipitously as the technology becomes more widely applied. Second, the technology is the limiting factor in many cases, once the technology is fully understood, the potential products become almost infinite. Third, several of the organizations contacted in the course of investigation for this report were unwilling to disclose the specific disease organism or issue they were working on, for obvious commercial reasons. As a result, the discussion is on research direction and processes, and not on potential products resulting from the research process.

4.1 Immunization Modulation

Immunization modulation offers a great number of potential pathways for approaching animal husbandry issues including productivity, quality and animal health. It is also an area

where Canada also enjoys a significant degree of strength.

Immunization modulation refers to modulating the body's ability to resist infection or invasion by other agents or organisms, and to counter any harmful effects they may have. This has obvious applications in the area of disease control, but has significant applications where the antibodies formed as part of the immune response can be made to mimic hormones and enzymes needed to produce desired metabolic changes.

This area can be broken down into several subprocesses. These are: active immunization, including sub-unit and live vehicle vaccines, passive immunization, including monoclonal antibodies and anti-ideotype antibodies, and antibody development for use in rapid systems detection. These pathways are shown in Figure 4.1, and discussed in detail below.

Active Immunization

Active immunization is the process whereby exposure to disease organisms or foreign pathogens confers resistance to subsequent infection. In essence, the triggering mechanism (antigen) of the foreign body is recognized by the host, which manufactures a specific antibody which is capable of binding to the antigen and rendering it harmless, or assisting in the ingestion of the antigenic matter by phagocytes. The key to active immunization is in finding a way in which the body can be "trained" to develop an antibody for a specific disease, without actually infecting it with the disease. The major benefit of active immunity compared to passive immunity (discussed below), is that the effects are generally much longer lived

Biotechnology offers the potential for radically new approaches to active immunization through two main processes. These are:

Sub-unit vaccines

Sub-unit vaccines are manufactured when the molecule (subunit) that is needed to elicit the proper immune response is isolated and reproduced. By administering only the sub-unit, the pathogenic properties of the entire organism are avoided, while at the same time, the organism, in response to the sub-unit, develops the antibodies

necessary to provide immunity.

These sub-unit molecules can be produced either synthetically, or through the use of recombinant DNA technology.

Live vehicle vaccines

Live vehicle vaccines are made when the molecule (sub-unit) that is needed to elicit an immune response (antibody development) is transferred from the pathogenic organism (virus, bacteria, or parasite), and transferred to an innocuous organism which can act as a carrier (this organism may also be a virus or bacteria, but one with no pathogenic properties). This organism is then able to replicate itself as a means of producing the product.

The major benefit of a live vehicle vaccine is that it is theoretically possible to use a single virus or bacterial vehicle to exhibit a number of antigens. Thus, a multivalent vaccine could be produced. Through a single vaccination, a number of different diseases could be controlled, or so could complex diseases (such as shipping fever) which are caused by a number of different vectors.

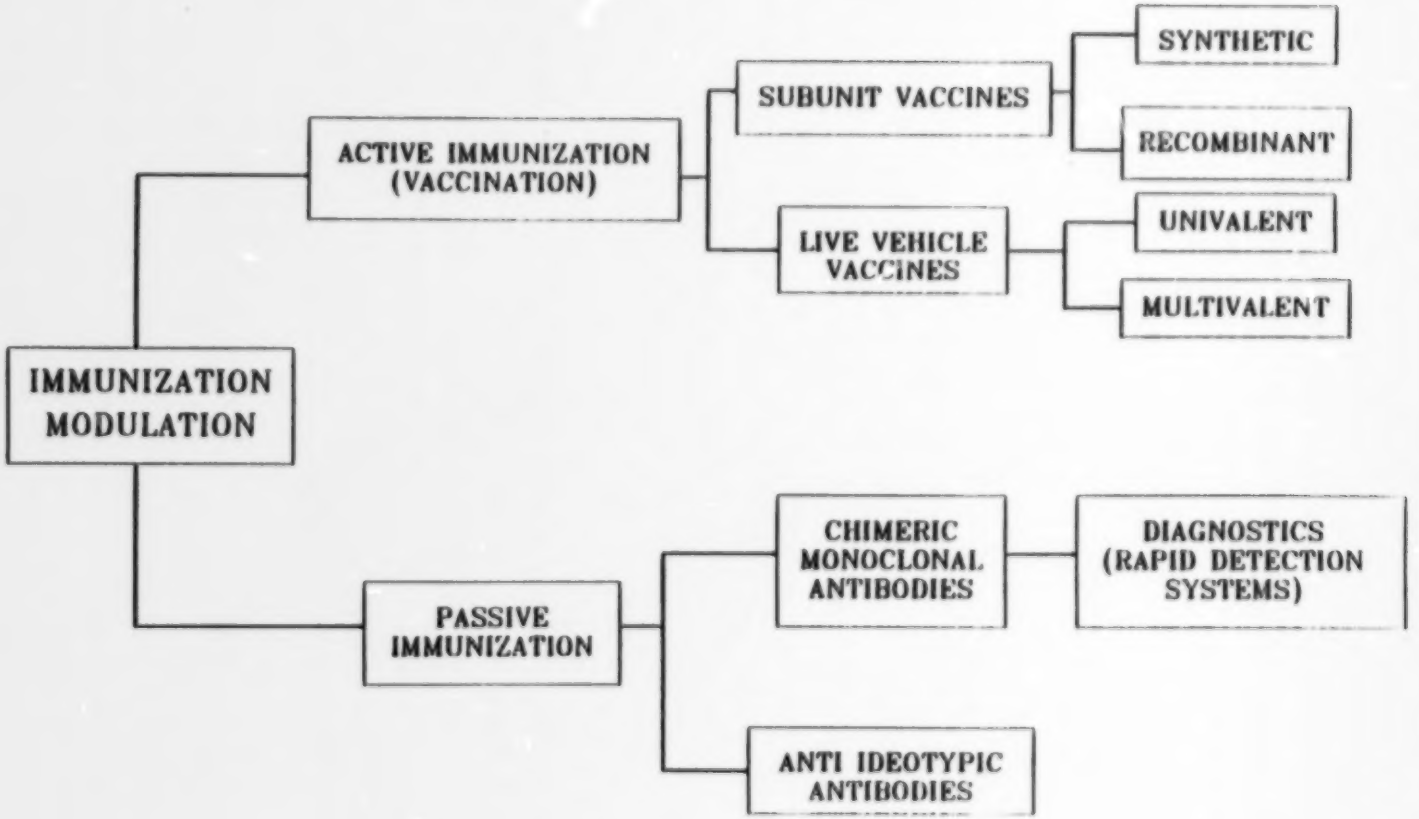
Research is currently being conducted into both of these areas in Canada. The major pathogens targeted are:

- those making up the shipping fever complex
- rotovirus and coronovirus (causes scours)
- pleuropneumonia
- infectious bovine rhinotracheitis

Anti-parasitic vaccines are allso under development.

Multivalency is most likely to be achieved at first by mixing of different viral or bacteria, each expressing specific antigens. Subsequently it is hoped that a single virus or a single bacteria could express all of the required antigens. Multivalency of the first type is already here, but that of the second type is still several years away at a minimum.

FIGURE 4.1
MAJOR PROCESS IN IMMUNIZATION MODULATION



Passive Immunization

Passive immunization is the process by which the organism is provided with the appropriate antibodies to bind with the target. When the target is a pathogen, the organism is protected from disease. However, when the target for the antibody is the binding site of a hormone, enzyme or toxin, a number of metabolic and physiologic impacts can be affected both beneficially or detrimentally. The main advantage of passive immunization is that allows the farmer to use a disease control only if when and if it occurs, thereby reducing costs and reducing stress on the animal by handling or needling only when necessary. There are two main biotechnical processes through which passive immunity can be achieved, the development of chimeric monoclonal antibodies, and anti-ideotypic antibodies. These are described below.

Monoclonal antibodies

A monoclonal antibody is a specific antibody derived from one of numerous identical cells derived from a single parent cell. The target antibody can be achieved through screening of hybrid cell cultures (the traditional method), or manufactured by implanting the necessary genetic material into the parent cell to produce the antibody of choice. The major advantage of monoclonal antibodies is the ability to produce large volumes of very high purity product.

Monoclonal antibodies have to date only been manufactured in mice. The difficulty lies in developing a species homologous antibody which were work in large animals.

Current research in Canada is on Bovine Rhinovirus and Leptospirosis.

Diagnostics

Another use of monoclonal antibodies in the development of rapid detection systems. This use requires absolute specificity, which is achievable only through monoclonal procedures. It has significant benefits to the animal husbandry sector through improving the reliability of diagnosis, and hence reducing can help to

reduce overall costs of disease control. Current research in Canada is focusing on systems for detecting listeria and coronovirus, as well as markers for identifying whether dairy animals have been treated with BST.

Anti-ideotypic antibodies

Anti-ideotypic antibodies are antibodies which mimic hormones, enzymes, toxins, microbes and receptors. The implications for their use are enormous as they can potentially block or enhance virtually any process that is affected by the product which they are mimicking. Potential uses include passive immunity, physiological regulation, therapy, drug design and delivery. Research in this area is still relatively preliminary, and no specific products are on the horizon as yet.

4.2 Chemical Modulation

Biotechnical chemical modulation is the process of producing a chemical through biotechnical processes (usually recombinant DNA technology applied to common microbes) to produce a chemical that is able to act on metabolic processes, disease organisms or can alter the structure/composition of animal inputs such as feed. The major research in Canada relates to three general areas:

1. development of products to regulate metabolic processes. Currently research is being conducted into the potential for products to regulate the production of Bovine and Porcine somatotropin. Another area is in the development of Beta-agonists, for use as repartitioning agents to improve both growth and meat characteristics.

2. modification of the rumen bacteria in bovine species. This can have beneficial results in three ways including microbes which are themselves more nutritious to the animal, microbes which secrete chemical which have a beneficial effect, and microbes which are capable of breaking down alternative feedstuffs through the production of different enzymes.

3. modification of microbes for use in treating feed external to the animal. Yeasts and

bacteria are being examined to select for suitability for application to feed stuffs to achieve the same objectives as above. The major benefit would be the ability to apply the benefits to non-ruminants.

4.3 Transgenics

The potential possibilities for approaching animal husbandry issues through the use of transgenics are almost limitless. The ability to make the animal perform the necessary metabolic or immunization procedures without resorting to administration of vaccines, growth promotants or other external stimuli will have enormous benefits in terms of the cost of production, increased productivity and reduced animal stress and operator labour.

While the potential for transgenics is great, in practice, it will be some years before this potential is realized. The closest "product" is the use of eukaryotic expression systems to manufacture human proteins and express them in the milk of dairy animals. A number of major technical problems need to be worked out, including developing a more complete understanding of DNA profile for the animal species in question. In the area of developing genetic resistance this is a particular barrier, as most factors of resistance are polygenic in nature, and require not only an understanding of where the genes are located, but of the interaction of the genes as well.

While the major step in transgenics is learning how to manipulate the genetic material, of almost equal importance is the need to develop mechanisms to replicate those desired characteristics in the animal population. This is the area of embryo biotechnology, and offers significant opportunity for Canada, based on the advanced state of our knowledge, raw materials and infrastructure relative to other countries.

Cloned embryos as a product, whether transgenic or not, will have a profound effect on the animal breeding industry. They will almost certainly eventually replace semen as the traded commodity in breeding and production.

For this to occur, further research is required in 6 major areas, all of which are areas of research within one or several Canadian institutions. These areas of research are:

Superovulation:	the process of stimulating the production of, and collecting large numbers of embryos.
In-vitro fertilization	studies to increase the efficiency of conception.
Embryo sexing	development of methods to predict the sex of the embryo at the earliest possible stage.
Cloning	development of methods for splitting the embryo to provide clones of genetically identical animals.
Preservation	development of methods to preserve the embryo over time so that a "bank" of genetic material will be available for reproduction should the original animal prove to be superior in the desired traits.
Enhancing survivability	survivability of the embryo after implantation is a problem. Further research into causes and potential treatments of embryo mortality are required.

5.0 INITIAL ASSESSMENT OF MARKET OPPORTUNITIES

This chapter provides an initial overview of some of the commercial opportunities in the animal husbandry biotech area. An opportunities assessment framework is outlined which is used to indicate potential opportunities. As well, the gross benefits of technological improvement are examined, and some of the constraints to development are noted. This chapter also contains a case study of BST, which is used to highlight some of the implications of commercialization of biotech products. Finally, the chapter summary presents some of the product areas which appear to have high potential for commercialization.

5.1 Opportunities Assessment Framework

Chapter 4 identified 11 biotechnical mechanisms which may yield an almost infinite variety of products/applications. These processes are:

1. sub-unit vaccines;
2. univalent live vehicle vaccines;
3. multi-valent live vehicle vaccines;
4. monoclonal antibodies;
5. anti-ideotypic antibodies;
6. rapid detection systems;
7. chemical metabolic regulators;
8. modified microbes (internally applied);
9. modified microbes (externally applied);
10. transgenics;
11. enhanced embryo transfer techniques.

The framework used to provide an initial assessment of opportunities in the animal husbandry biotech sector includes three major components:

- an estimate of the size or importance of the market;
- an analysis of the availability of current solutions;
- an estimate of the potential for, and constraints on a viable biotech solution.

5.2 Gross Benefit of Technological Change

This section attempts to place in context the potential benefits that may arise in the domestic livestock sector due to the introduction of new animal husbandry products. In so doing it shows the potential for value added in the animal health products manufacturing sector.

The methodology used was to address a number of the issues from Chapter 3, and postulate the gross economic benefit to the domestic livestock production sector if an improvement where to be made. The specific issues addressed and assumptions made are as follows and are summarized in Table 5.1.

5.2.1 Beef Sector

Beef - Economic benefit of improvement in feed efficiency

Feed costs are the most significant cost category in the beef finish enterprise. Data compiled by the Ontario Ministry of Agriculture and Food (OMAF, Ontario Farm Management Analysis Project, 1988. Publication 69) estimates the feed cost (not including additives) for raising a 600 pound animal to market weight at $252.00. If costs are assumed to be similar for the rest of Canada, then the total feed costs for fed cattle in Canada would equal 2,363,678 x $252.00 or 595 million dollars. It can easily be seen that any product that improves feed efficiency will have demonstrable benefits to farmers. Every 1% gain in efficiency would be worth $5.95 million to the beef finishing sector.

The benefits from reducing the cost of feed through substitution of alternative feeds would have a similar benefit as above.

Table 5.1 Potential Domestic Benefits of Technological Change in Animal Husbandry Issues

Issue		Cost Areas Affected	Total Cost to Industry ('000s of dollars)	Gross Value of 1% Improvement ($'s)
Beef				
	Feed Efficiency	Feed Costs	595,000	5.95 million
	Rate of Gain	Overhead and Interest Costs	250,000	2.5 million
	Carcass Quality	Meat Prices	2,159,211	21.6 million
	Animal Health	Veterinary and Medicines	30,000	.3 million
Hogs				
	Feed Efficiency	Feed Costs	725,000	7.25 million
	Rate of Gain	Overhead and Interest Costs	219,000	2.19 million
	Carcass Quality	Meat Prices	1,548,000	15.5 million
	Animal Health	Veterinary and Medicines	28,300	.28 million
Dairy				
	Feed Efficiency	Feed Costs	1,870,000	18.7 million
	Animal Health	Veterinary and Medicines	113,000	1.1 million

Beef - Economic benefit of improvement in rate of gain or days to market

Reducing the number of days it takes to raise an animal to market weight has two beneficial impacts. First, it reduces the cost of capital required to finance the cattle, and second, if we assume that capacity utilization is constant, i.e. as finish cattle are moved out, replacements are brought in, then the fixed costs of the operation will be spread over more cattle and per unit costs will be lowered. OMAF data shows average total fixed costs per head to be $102.56 for raising a 600 pound animal to market weight. Using the same logic as in the example above, it can be shown that the total annual fixed costs for the Canadian industry are approximately $250 million. Expressed in another way, the average beef animal takes just over 300 days to go from 600 to 1200 pounds. Every day which can be saved is worth just under $1 million cumulatively to the Canadian industry.

Beef- Economic benefit of an improvement in carcass quality

Carcass quality improvements may contribute to increased returns to the production and packing sector in two ways. first, increasing the relative yield of higher valued portions such as lean meat, and second, by improving the characteristics of the meat such as texture, type of protein or fat, such that the consumer is willing to pay more for the product.

Canadian average wholesale prices for dressed beef carcasses in 1989 were approximately $3.30 per kilogram for A1 and A2 steers and heifers. Total production of carcass beef from these sources comes to 654 million kilograms. If a benefit of 1% improvement in the wholesale value of high grade beef were assumed, the benefit to the production and packing sector would equal approximately $21.6 million per year for the country, not including the increased value of exported livestock.

Beef - Economic benefit of a decrease in veterinary and medicine costs

The benefits to increasing the level of health are difficult to measure. This section quantifies the expenditures on veterinary fees and medicines, however the major benefit probably lies in reducing the economic cost associated with diseases for which there is currently no adequate control. For instance, the total yearly North American expenditures on animal health products is estimated at $2.45 billion, but the economic losses related to

diseases in animal husbandry is estimated to be near $20 billion annually. Figures for Canada alone are not available.

The economic benefit to the beef finishing industry in Canada from would be approximately $.3 million for each 1% reduction in costs.

5.2.2 Hog Sector

The potential benefits of biotechnology in the hog sector are similar in form to those in the beef sector. This section quantifies these potential benefits utilizing the same logic and rationale as was used above. The analysis for hogs examines only the hog finishing enterprise, except for the section on veterinary and medicine, which considers the entire life cycle.

Hogs - Economic benefit of improvement in feed efficiency

Feed costs per market hog averaged $51.27 in Ontario in 1988. This figure can generally be considered an average cost for the country, as Quebec and Atlantic Canada costs are somewhat higher, and Western Canada costs somewhat lower. Total expenditures on feed equal $51.27 x 14.2 million finish hogs marketed, or $725 million. Thus, every one percent improvement in feed efficiency would lead to a gross benefit of $7.25 million dollars across the Canadian hog finishing sector.

Hogs - Economic benefit of improvement in days to market

Average fixed costs per market hog in finishing operations equals $15.42, for a total cost to the industry of $219 million. The average number of days from grower hog to market for the finishing enterprise is 132. Hence, every day that can be saved would be worth $1.7 million cumulatively to the Canadian industry.

Hogs - Economic benefit of an increase in carcass value (due to quality improvement)

Average prices for dressed hog carcasses (Toronto) were $1.38 per kilogram. Average carcass weights for Canada were 79 kilograms, and 14.2 million hogs were marketed.

Hence, the total wholesale value of pork marketed for 1988 equalled $1.548 billion. Every 1% gain in the average wholesale market value of the carcass would be worth over $15 million to the industry.

Hogs - Economic benefit of a decrease in veterinary and medicine costs

Swine veterinary costs averaged $29.80 per sow in 1988. The total number of sows in Canada is approximately 950,000. Therefore, the total expenditure on veterinary and medicine (not the total cost of disease) is approximately $28.3 million.

5.2.3 Dairy Sector

The economic benefits of biotechnology to the dairy sector are somewhat more difficult to quantify given the nature of dairy production in Canada. Under the supply management system total output is constrained, and opportunities for diluting fixed costs at the industry level are limited. Even calculating the benefit to an increase in productivity is complicated by the fact that if each cow produces more milk, then fewer animals are needed to fill quota requirements, and the cows that are left ~~much~~ must each assume a higher share of the farm overhead.

This section examines only the impact of reducing feed costs, and the impact of reducing vet and medicine costs. The BST case example presented later in this chapter presents some other insights into the benefits of biotechnology in a supply managed situation.

Dairy - Economic benefit of an improvement in feed efficiency

Average feed costs per producing dairy cow in Ontario were $1,296 in 1988. Feed costs in Ontario are typically higher than those in Western Canada but lower than in Quebec and the Maritimes, so should serve as a rough average. The total number of dairy cows in Canada, as of July 1, 1988 equalled 1.44 million. Total feed costs in the sector equalled $1.87 billion. Every 1% reduction in the value of feed needed to achieve the same level of output would have a gross benefit of $18.7 million cumulatively to the dairy producers.

Dairy - Economic benefit of a decrease in veterinary and medicine costs

Average vet and medicine costs in Ontario equalled $78.81 per cow in 1988. If we assume that this cost would be similar for the rest of Canada, the total vet and medicine cost would be $113 million. The 1% benefit would therefore be $1.1 million.

5.3 Product/Process Constraints

This section examines some of the constraints on developing biotech products for use in animal husbandry. All of the mechanisms listed in section 5.1 have the potential to produce viable commercial products. However, at this point there are no commercially available products in the animal husbandry sector which rely exclusively on biotech solutions.

A number of products are currently in various stages of development. At best, some are awaiting only regulatory approval before introduction (BST), other mechanisms have not yet produced a product, and are still in a largely theoretical stage (transgenics).

Table 5.2 summarizes the research and development stage of the products mentioned in Chapter 4. There are three categories used to describe degree of product development:

Product Stage - refers to a case where a specific product has been developed and is in a marketable form.

Development Stage - refers to a case where a specific market opportunity has been targetted, but where further research and development is necessary before a product can be brought to market.

Theoretical Stage - refers to a case where research is being persued on topics where there is no direct market opportunity, i.e. where the ground work for future commercial applications is being laid.

It should be emphasized that virtually all biotech research has a strong theoretical component, but not necessarily exclusively so.

TABLE 5.2 BIOTECH PRODUCT RESEARCH STAGES

MECHANISM	PRODUCT	RESEARCH STAGE		
		PRODUCT STAGE	DEVELOPMENT STAGE	THEORETICAL STAGE
SUB-UNIT VACCINES				X
UNIVALENT LIVE VEHICLE VACCINES	ROTO AND CORONOVIRUS		X	
	PLEUROPNUEMONIA		X	
	IBR		X	
	PASTEURELLA	X		
	ANTI-PARASITICS		X	
MULTI-VALENT LIVE VEHICLE VACCINES	SHIPPING FEVER COMPLEX		X	
MONOCLONAL ANTIBODIES	BOVINE RHINOVIRUS		X	
	LEPTOSPIROSIS		X	
ANTI-IDEOTYPIC ANTIBODIES				X
RAPID DETECTION SYSTEMS	LISTERIA		X	
	CORONOVIRUS		X	
	BST MARKERS	X		
CHEMICAL METABOLIC REGULATORS	SOMATOTROPINS	X		
	BETA-AGONISTS	X		
MODIFIED MICROBES (INTERNAL)			X	
MODIFIED MICROBES (EXTERNAL)			X	
TRANSGENICS	TRANSGENIC ANIMALS			X
	EUKARYOTIC EXPRESSION VECTORS		X	
ENHANCED EMBRYO TRANSFER TECHNIQUES	CLONED & SEXED EMBRYO		X	

5.4 BST - A Biotech Example

Section 5.2 of this chapter served to highlight some of the potential benefits which may occur through use of biotechnology. This section serves to qualify some of those benefits by looking at a specific example, namely, Bovine somatotrophin (BST).

The prospective introduction and adoption of BST in Canada has a number of ramifications within the dairy industry above and beyond an increase in productivity and efficiency of milk production. A recent study of these issues[1] identified some of the following impacts:

1. For the average cow administered BST, milk production would increase by 4 kg/day, or 12-15%.

2. After 10 years, 50 to 75% of Canadian producers would adopt the technology. They would use it (after proven conception) on 60 to 80% of their cows for 75 to 90% of the eligible application period. This translates into the equivalent of 20 to 50% of all cows would recieve BST for the full eligible application period.

3. Consequently, BST should increase overall milk production by 3 - 8% and given current supply management arrangements, reduce the dairy cow population by 3 - 8%.

4. The adoption of BST would incur some direct increases in feeding and production costs for the dairy herd, and reduced revenues from sale of surplus and cull animals. Moreover, increased efficiencies of production would result in price reductions paid to farmers for their milk consistant with the cost of production formula and pricing arrangements for milk. Additionally, producers would be faced with higher costs for quota.

5. The net benefits of BST at full adoption would be of the order of 3 to 4% of gross income for adopting producers, and from -1 to -3% for non-adopting producers.

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[1]BST in Canada - Projected Farm Level and Industry Impacts and Potential Adoption Scenarios. Deloitte & Touche, March 1990

These benefits would translate into aggregate benefits to producers in the order of 30 to 60 million dollars, with equivalent levels of benefit to consumers. Additionally, the value of the product to the veterinary supply and manufacturing sector would be of the order of 15 to 30 million dollars. This level of benefit would be accompanied by some positive benefits to the feed sector and negative effects on the breeding, semen and veal calf sectors.

This product also highlights another general issue of biotechnology, which is the potential difficulty of obtaining consumer acceptance with a product based on high technology. The average consumer does not understand the process and cannot evaluate it relative to older technologies.

6.0 SUMMARY

The objectives of this phase of the research were:

1. to identify and list the major issues/products/techniques of significance to the biotech industry; and

2. to provide an initial assessment of the commercial significance of these areas and desirability of further research.

Chapters 3 and 4 of this report addressed the first objective, while Chapter 5 addressed the objective 2. One of the greatest difficulties is in assessing the product opportunities. Biotechnology tends to be process driven, i.e. essentially the same process or mechanism can be used to develop or manufacture a number of different products. However, commercial opportunities are based on products. Therefore, an assessment of commercial significance requires first that the technology or process be viable, and second, that ti be directed towards significant market opportunities.

Discussions with researchers involved lead us to believe that technical viability can be achieved in all of the areas mentioned, but success will come sooner in some areas than others.

In the short term, (1 to 3 years), the most significant potential appears to be in the area of live vehicle vaccines, and embryo transfer. Both of these areas have definable products, high commercial value, and few replacements. Additionally, further research in these areas will possibly lead to developments in the areas of multi-valent vaccines and transgenics respectively.

The greatest potential benefits to the Canadian biotech sector are not necessarily in the short run. Multi-valent vaccines, monoclonal antibodies, and transgenics have huge commercial potential, which is at this time limited by a number of technical barriers.
Over the longer term it is much more difficult to predict where the significant opportunities exist. The nature of biotechnology research at this stage is that many of the most important discoveries and applications occur as spin-offs to the main research. Hence, there is still a

need to undertake longer term research with less potential for immediate payback.

This serendipitous aspect to new product or process discovery, as well as the need for a multidisciplinary approach to biotechnology point to the need for strong industry concentration, communication and linkages. The framework for Phase II research outlined in the next chapter discusses how this may be accommodated within the objectives of further qualifying the development potential and opportunity areas for animal husbandry biotechnology.

7.0 A FRAMEWORK FOR PHASE II

The following is based on an understanding that in Phase II of this project, the following objectives will be addressed:

1. to provide a framework to guide policy making concerning the biotech industry;

2. to identify appropriate roles for government in the biotech industry, and the associated nature of government programming; and

3. to address the issue of what factors must be present to ensure a probability of success of their being a competitive world class biotech industry in Canada.

Addressing the first two objectives in a satisfactory manner is entirely dependent on the findings associated with objective three.

Furthermore, it is also understood that Phase II will use case studies of specific opportunity areas which will help address these objectives.

7.1 A Suggested Case Study/Bio-Tech Framework

A framework is necessary to guide conduct of the case studies. The issue of what are the necessary factors required for having a sustainable biotech industry is very similar to the issue of market place competitiveness. To be competitive implies that an industry is maintaining or expanding its share in a market, domestic and/or foreign. Being competitive is similar to the issue of will an industry survive and thrive. This is the issue for the biotech sector in Canada.

As identified by Deloitte & Touche for the Task Force on Competitiveness in the Agri-Food Industry, competitiveness is not one-dimensional, and is not based on being the lowest cost producer. Rather successful industries are based on a myriad of factors, ranging from positive entrepreneurial attitudes, to partnerships with customers and

suppliers, to understanding the nature of demand, to having appropriate human resources in the industry, to exporting strengths developed in the domestic market. Synergies with associated industries, such as universities, input suppliers, customers and related industries were also extremely important. A successful and competitive industry depends on a complex set of interrelationships.

For Phase II, a framework that will help address the research objectives will include the following:

1. FACTOR CONDITIONS

   This relates to the factors needed to be in the biotech business. They range from scientist, to process equipment, to laboratories, etc.

2. RELATED & SUPPORTING INDUSTRIES

   This is a key area in biotech and in many emerging industries. This includes private, public, and university R&D on biotech, and biotech process. Included is research in related fields such as human genetic research, etc. supporting and relating industries also includes the pharmaceutical companies that are investing in comparable technological processes.

   Canada's experience in embryo transplants, genetic exports, etc. also are supporting the development of a biotech industry.

   Supporting industries would also include the distributors of animal health products, including the veterinarians and their animal health programs. Packaging companies should also not be ignored, and a comparison to competing nations is also a requirement in this area.

3. DEMAND CONDITIONS

   Early in this report, the domestic demand potential was identified. Many successful new or emerging industries are based on satisfying upscale demands and market needs in a domestic, or local context, and then satisfying similar needs in a broader context (world market).

   Understanding the exact nature of demand is important, since a heavy investment is likely required in the production process to develop the animal health product.

Canada does have a good domestic demand environment with a focus on safety and animal health. The regulatory environment may add to the success, or totally impede progress.

4. COORDINATION, COOPERATION AND COMMUNICATION

The biotech industry can cover many industries within a sector, and activities should be coordinated.

A low probability of success can be guaranteed if information links and partnerships do not develop between all facets of the sector. From the university, to the biotech process facility, to the distributor, to the veterinarian to the ultimate customer, the farmer.

5. GOVERNMENT

Government directly and indirectly can foster a biotech industry. This ranges from associated support at universities, its involvement in public research, and the regulatory environment. Tax incentives, etc. that are targeted to biotech can also stimulate the process side of the business.

6. OVERALL BIOTECH SYNERGY AND CRITICAL MASS

The ability for Canada to sustain a world class biotech industry will result from sufficient strengths and critical mass in each of the above five areas. Only then will there be sufficient synergy to have a successful biotech industry. The important caveat is that other competing countries are not out of the barn door earlier, or too early, relative to Canada's charge.

7.2 Phase II Strategy

The following approach is suggested for Phase II:

1. Formalize the above framework and modify it for the particulars of biotech and emerging industries;

2. Develop case study instruments to guide the conduct of the case studies which incorporates the framework of Phase I above;

3. Conduct the strategically chosen case studies (potentially three) and provide individual case study reports;

4. Synthesize results of the case studies;

5. Draw implications relative to the three objectives presented; and

6. Present results to the client and to a larger biotech forum.

Deloitte & Touche

ÉTUDE DE POSSIBILITÉS STRATÉGIQUES POUR LA BIOTECHNOLOGIE CANADIENNE DANS LE SECTEUR DES PRODUITS DE ZOOTECHNIE

Rapport sur la Phase I

SOMMAIRE

1. Les avantages potentiels de la biotechnologie dans le secteur de la zootechnie représentent des milliards de dollars. Lorsqu'on considère les retombées de la recherche, soit l'application éventuelle de techniques similaires à d'autres espèces, y compris les humains, les avantages potentiels augmentent considérablement.

2. En ce qui concerne les produits biotechnologiques du secteur de la zootechnie, les applications potentielles sont pratiquement illimitées. Les principaux domaines d'application sont les suivants : contrôle des maladies, résistance à la maladie et amélioration des capacités et caractéristiques de production.

3. Ces énormes avantages économiques sont mitigés par le coût élevé de la recherche et de la mise au point des produits. Dans le secteur de la biotechnologie, les coûts sont beaucoup plus élevés que dans la recherche conventionnelle. La disponibilité du capital est un des principaux facteurs limitatifs pour les entreprises et institutions de recherche en biotechnologie.

4. Le Canada est un chef de file dans divers domaines de la biotechnologie, et particulièrement dans ceux des techniques d'embryologie et d'immunisation.

5. Peu de produits biotechnologiques sont actuellement prêts à être commercialisés. La plupart des recherches se concentrent encore sur la compréhension des processus, la crtographie des gènes et l'établissement de bases pour des applications particulières.

6. Pour que l'industrie se développe dans son ensemble, et que le Canada joue un rôle important, il sera nécessaire d'adopter une approche résolument multidisciplinaire et d'atteindre un haut niveau de coordination industrielle.